

Appl. No. 10/052,362
Atty. Docket No. CP-1218
Amtd. Dated January 9th, 2004
Reply to Office Action of October 9th, 2003

has been placed in independent form per the Examiner's instructions. No new matter has been added. No additional Claim fee is due.

Claims 1-10 have been rejected under 35 U.S.C. §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the Examiner has rejected the language "R³ and R⁴ together form a C₁ to C₅ alkylene group". The Examiner has correctly identified that Applicants have incorrectly stated that C₁ may be an alkylene group. One of ordinary skill in the art will immediately recognize that there must be at least 2 carbon atoms present for an alkylene group to exist. As such, one of ordinary skill in the art would recognize that the phrase should read "C₂-C₅ alkylene group" Accordingly, the correction does not constitute new matter. As such Applicants have made a correction to both the specification and the claims to correct this obvious error.

Claims 1-6 have been rejected under 35 U.S.C. §103(a) as being unpatentable over the article by Coleman et al entitled "Nicotine-like Stimulant Actions of Several substituted Phenylcholine Ethers" in view of an excerpt from the book "Organic Chemistry" by Bruice. Applicants respectfully traverse the rejection.

The Coleman reference teaches substituted phenylcholine ethers which display nicotine like stimulant action. However, as the Examiner recognizes, Coleman does not teach or discloses the compounds claimed by Applicants. Namely, Coleman fails to teach a substituted amino group in the meta position of the phenylcholines set forth. Rather, Coleman teaches only non-substituted amino. The Examiner then weaves a complex path through the organic chemistry world in order to arrive at a motivation to modify the teachings of the Coleman reference. The Examiner draws teachings from the Coleman reference that teach that the inductive effect or electron withdrawing is what plays a role in increasing the activity of a compound's nicotine like stimulant ability. And further that the electron resonance effect or electron donating has a negligible effect on the activity.

The Examiner then cites the Bruice reference as showing that NH₂ set forth in Coleman a more strongly activating substitution than NR₂ as claimed by Applicants. Thus, as NR₂ has a better inductive effect than NH₂ per the table in Bruice and Coleman teaching inductive effect is what plays a role in activity for nicotine like stimulant ability than it would be obvious to one of ordinary skill to modify Coleman to arrive at the NR₂ group claimed by Applicants.

However, in so crafting the above line of reasoning to establish motivation, the Examiner has ignored the clear teachings of the combination as a whole to arrive at Applicants invention. When examined as a whole, the combination of references fails to provide the stated motivation.

The teachings of Coleman lead one of ordinary skill in the art to conclude that the substitutions which have a stronger inductive effect than resonance effect provide greater activity

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to the compounds disclosed. At the same time, substituents which provide too strong an inductive effect such as the nitro group are very poor performers. Thus, Coleman concludes that inductive effect alone is not the answer. Rather some other effect is at work, namely polarizability or inductometric effect. This is the ability of the inductive effect along the substituent and ring bond at the moment of interaction with a second molecule. Thus, a substituent which increases this effect is the preferred substituent. Coleman goes on to state that electronegative effect plays a role. This is demonstrated by the halogens where a weakly electronegative substituent such as I is the most activating. Thus, Coleman et al's teachings lead one of ordinary skill in the art to conclude that a substituent which has an inductive effect yet weak electronegativity is actually the preferred substituent. This is confirmed by Coleman wherein, the I group is the most activating group, even more so than the NH₂ group (see page 70). Presumably then Coleman's preferred compound would be I substituted phenylcholine ether.

Thus, one of ordinary skill in the art concludes that a compound which is both weakly electronegative and more strongly inductive will be a better activator for the nicotine like stimulants of Coleman. One of ordinary skill in the art is also well aware that substituents such as N are more greatly electronegative than those of C or carbon. Thus, one of ordinary skill would be motivated to choose a more inductive C substituent from the list in Bruice rather than the N substitution set forth by the Examiner. The Examiner has seized upon and selected the NR₂ substitution from the more than 20 potential substituents in Bruice as it is the only one from the list in Bruice which potentially reads upon Applicants claims. However, the clear teaching to one of ordinary skill in the art from the combination of Coleman and Bruice are substitutions combining both weak electronegativity and inductive effect of which there are a number of better options from the list in Bruice than NR₂ namely a number of different C substituent options, including a straight C chain. Clearly, when viewing the combination as a whole the motivation set forth by the Examiner breaks down and is found lacking. One of ordinary skill in the art is in fact lead aware from the asserted modification set forth by the Examiner and lead in an entirely different direction. Accordingly, the Examiner has failed to establish a prima facie case of obviousness in the asserted combination and the claims as amended are novel and unobvious over the prior art of record.

Conclusion

In light of the remarks presented herein, Applicants' respectfully submit that Claims 1-10 are allowable over the prior art of record or any combination thereof. Reconsideration and reexamination are respectfully requested. In the event that issues remain prior to allowance of the

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noted claims, then the Examiner is invited to call Applicants' undersigned attorney to discuss any remaining issues.

Respectfully submitted,

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